IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Santos Savio et al.	Examiner:	Bruce D. Hissong
Serial No.:	10/529,923	Group Art Unit:	1646
Filed:	August 29, 2005	Docket:	976-24 PCT/US/RCE III
Confirmation No:	5270	Dated:	March 11, 2009
For:	VACCINE COMPOSITION COMPRISING INTERLEUKIN-15 (IL-15)		

Board of Patent Appeals and Interferences
United States Patent and Trademark Office
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(Printed Name)

APPEAL BRIEF PURSUANT TO 37 C.F.R. §41.37

Sir:

This is an appeal to the Board of Appeals from the examiner's rejection of Claims 22 and 23 in the Office Action mailed October 16, 2008. A timely Notice of Appeal was filed on January 16, 2009.

I. REAL PARTY IN INTEREST

The real parties in interest are:

Centro de Ingenieria Genetica y Biotecnologia.

II. RELATED APPEALS AND INTERFERENCES

No related appeals, interferences, or judicial proceedings are known to Appellants or Appellants' legal representative which may be related to, directly affect, or be directly affected by, or have a bearing on, the Board's decision on this appeal.

III. STATUS OF CLAIMS

The status of the claims in this application is:

A. Total Number of Claims in Application

Claims in the application are: Claims 1-23.

B. Status of all the Claims

1. Claims cancelled: 1-21.

2. Claims pending: Claims 22-23.

3. Claims allowed: None.

4. Claims rejected: Claims 22-23.

C. Claims on Appeal

The claims on appeal are: Claims 22-23.

IV. STATUS OF AMENDMENTS

A final Office Action was mailed on April 4, 2007. The Office Action rejected Claims 14-22 newly submitted in the previous Amendment. Claims 1-13 had been cancelled. In response, Applicants submitted a Response to Final Office Action, a Request for Continued Examination (RCE) and the requisite fee. In the response after final, Applicants made various amendments to Claims 14-17, 20 and 22. Applicants added new Claim 23 and cancelled Claims 18, 19 and 21.

A second Final Office Action was then mailed on October 18, 2007 finally rejecting Claims 14-17, 20, 22 and 23. In response, Applicants filed another Amendment cancelling

Claims 14-17 and 20, while amending Claims 22 and 23. Applicants also filed a second RCE in response to the second Final Office Action.

A third Final Office Action was then mailed on March 26, 2008. In response, Applicants filed another Amendment on June 26, 2008 amending Claim 22. Claim 23 was not amended. In response to the Amendment, Applicants received an Advisory Action mailed on July 30, 2008, advising that the Amendment filed on June 26, 2008 was not entered because it did not place the application in better form for appeal by materially reducing or simplifying the issues for appeal. Therefore, in order to have the Amendment originally filed on June 26, 2008 considered, Applicants file a third RCE on August 12, 2008.

On October 16, 2008, the examiner mailed a non-final Office Action again rejecting Claims 22 and 23. A Notice of Appeal was timely filed on January 16, 2009.

Accordingly, Claims 22 and 23, now being appealed, have been twice rejected. Therefore, Applicants appeal of Claims 22 and 23 is timely under 37 C.F.R. §41.31(a)(1).

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

Claim 22, the only independent claim on appeal, is set forth below:

> 22. A method for generating a neutralizing antibody response against autologous IL-15 in a primate, wherein said method comprises administering to said primate a composition comprising human IL-15 and aluminum hydroxide, wherein the IL-15 is an antigen and wherein said IL-15 antigen generates neutralizing self-antibodies against IL-15.

The claims comprise the following elements, each of which is followed by a reference to the specification by page and line number.

Element 1: A method for generating a neutralizing antibody

response against autologous IL-15 in a primate. (page 4, lines 19-25; page 5, lines 6-9; Example 2.)

Element 2: wherein said method comprises administering to said primate a composition comprising human IL-15. (page 5, lines 6-7; Examples 2 and 3.)

Element 3: and aluminum hydroxide. (page 1, lines 10-11.)

Element 4: wherein the IL-15 is an antigen and wherein said IL-15 antigen generates neutralizing self-antibodies against IL-15. (page 1, lines 6-8; page 4, lines 19-25; page 5, lines 6-7.)

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claim Rejection - 35 U.S.C. §103

Claims 22 and 23 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Grabstein et al. (WO 95/2772) in view of Gonzalez et al. (*Scand. J. Immunol.*, 2000, Vol. 52, p. 113-116), and further in view of Brewer et al. (*J. Immunol.*, 1999, Vol. 163, p. 6448-6454). According to the examiner:

> [O]ne of ordinary skill in the art would be motivated to create a composition comprising human IL-15 and aluminum hydroxide, and administer this composition to a primate because the skilled artisan would know that this composition and method would be useful in generating neutralizing antibodies useful for studying the biological actions of IL-15.

The motivation to do so comes from the disclosure of Grabstein, which teaches compositions comprising IL-15, and the disclosure of Brewer, which teaches the use of aluminum hydroxide to potentiate antibody responses after vaccination. Furthermore, because Gonzalez teaches conjugation to P64k as a method of increasing the immunogenicity of proteins, a person of ordinary skill in the art would be motivated to conjugate the P64k protein to human IL-15 because the skilled artisan would know that such a conjugate would more effectively generate neutralizing antibodies specific for human IL-15 when administered to a primate.

Thus, because one of ordinary skill in the art would know that a composition comprising human IL-15 and aluminum hydroxide would be immunogenic when administered to a primate, one of ordinary skill in the art would have both the motivation and the ability to administer a composition comprising human IL-15 and aluminum hydroxide, or human IL-15 coupled to P64k, to a primate for the purpose of generating neutralizing antibodies against IL-15. Because Grabstein describes the biological activities and potential pathogenic roles of IL-15, a person of ordinary skill in the art would be motivated to create neutralizing antibodies for the study of human IL-15 biological activities and properties.

VII. ARGUMENT

Background and General Description of Invention

The present invention relates to a method for generating a neutralizing antibody response against autologous IL-15 in a primate. Generating a neutralizing antibody response

against autologous IL-15 can be useful for the treatment of related diseases in which IL-15 is over-expressed. The method includes administering to the primate a composition that includes human IL-15 and aluminum hydroxide. When the IL-15 antigen is administered, it generates neutralizing self-antibodies against autologous IL-15 within the primate.

Rebuttal of Rejection of Claims 22 and 23 under 35 U.S.C. §103(a)-Obviousness

As stated above, the examiner asserts that one of ordinary skill in the art would be motivated to create a composition comprising human IL-15 and aluminum hydroxide, and administer this composition to a primate because the skilled artisan would know that the composition and method "would be useful in generating neutralizing antibodies useful for studying the biological actions of IL-15." The examiner concludes, "Because Grabstein describes the biological activities and potential pathogenic roles of IL-15, a person of ordinary skill in the art would be motivated to create neutralizing antibodies for the study of human IL-15 biological activities and properties." Applicants respectfully traverse this rejection and the reason behind it.

It is well settled that, to support an obviousness rejection, all words and claim must be considered in judging the patentability of that claim against the prior art. See *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 442 (CCPA 1970). Applicants respectfully assert that the obviousness rejection made by the examiner does not take into consideration all of the elements of the pending claims.

More specifically, Claim 22 relates to a method for generating a neutralizing antibody response against autologous IL-15. Claim 22 also states in the final "wherein" clause that the "IL-15 antigen generates neutralizing self-antibodies against IL-15." Accordingly, Applicants are not claiming the creation of any "neutralizing antibodies for the study of human IL-15 biological activities and properties" as suggested by the examiner. Applicants are claiming a method in which the administration of human IL-15 generates neutralizing

self-antibodies against IL-15. None of the cited references disclose or suggest this claimed method.

Grabstein, the main reference relied upon by the examiner, discloses in the Background of the Invention that T-cells, also known as T-lymphocytes, are a class of immune effector cells. These cells can be split into two general classes: T cytotoxic cells (T_c) and T helper cells (T_h). T_c cells are activated when they interact with an antigen-class I MHC complex on the surface of an altered self-cell in the presence of appropriate cytokines. T_h cells are activated by recognition of an antigen-class II MHC complex on an antigen-presenting cell. After activation, the T_h cell begins to divide and gives rise to a clone of effector cells, which secrete various cytokines, which play a central role in the activation of B cells, T cells, and other cells that participate in the immune response.

Grabstein discloses in the Background of the Invention that six T-cell growth factors had been previously identified: -2, -4, -7, -9, -12 and -10. Grabstein discloses in the Detailed Description that they identified a novel T-cell growth factor, referred to as IL-15. Grabstein discloses on page 4, lines 16-17 that IL-15 "is capable of signaling proliferation and/or differentiation of precursor or mature T-cells." Example 5 in Grabstein demonstrates the stimulation of CTLL-2 proliferation using IL-15. Accordingly, Grabstein concludes on page 24 that "one of ordinary skill in the art would expect IL-15 to stimulate the activity of CTL, LAK and NK cells and *expand* the population of T cells that can destroy tumor cells and viral-infected cells." [emphasis supplied]

The claimed invention, on the contrary, relates to a method for generating a neutralizing antibody response against autologous IL-15 in a primate. This generation of the neutralizing antibody response is shown in the examples which demonstrate neutralizing antibodies in monkeys' sera. More specifically, Example 2 demonstrates the increased level of anti-IL-15 antibodies in the monkeys' sera.

Instead of stimulating T lymphocyte proliferation as disclosed in Grabstein, the claimed neutralizing response would inhibit the activity of IL-15 as a cytokine, as disclosed

by Grabstein. The claimed neutralizing response is further demonstrated in the specification in Example 3, in which inhibition of IL-15 induced CTLL-2 proliferation was observed. Grabstein, on the other hand, demonstrates stimulation of CTLL-2 proliferation using IL-15.

It is well settled that a prior art reference must be considered in its entirety, i.e., as a whole including those portions that diverge from and teach away from the claimed invention. *W. L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F2d 1540, 1550, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Because Grabstein teaches the stimulation of T cell proliferation instead of the inhibition of T cell proliferation using IL-15, Grabstein teaches away from administering IL-15 to generate neutralizing self-antibodies against IL-15.

Conclusion

Applicant respectfully requests reversal of the rejection contained in the Office Action of October 16, 2008 for the reasons stated above. A check in the amount of $270.00 is enclosed herewith in accordance with 37 C.F.R. §41.20(b)(2). If any additional fees are due or an overpayment has been made, please charge or credit our Deposit Account No. 08-2461 for such sum.

VIII. CLAIMS APPENDIX

The claims involved in the Appeal are:

22. A method for generating a neutralizing antibody response against autologous IL-15 in a primate, wherein said method comprises administering to said primate a composition comprising human IL-15 and aluminum hydroxide, wherein the IL-15 is an antigen and wherein said IL-15 antigen generates neutralizing self-antibodies against IL-15.

23. The method according to claim 22, wherein the IL-15 antigen is coupled to a carrier protein, and wherein the carrier protein is P64k protein.

IX. EVIDENCE APPENDIX

No additional evidence is relied upon.

X. RELATED PROCEEDINGS

There are no Related Proceedings.

Respectfully submitted,

/james f. harrington/
James F. Harrington
Registration No. 44,741
Attorney for Appellant

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
Tel. (516) 822-2550
Fax. (516) 822-3582
JFH/lg

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